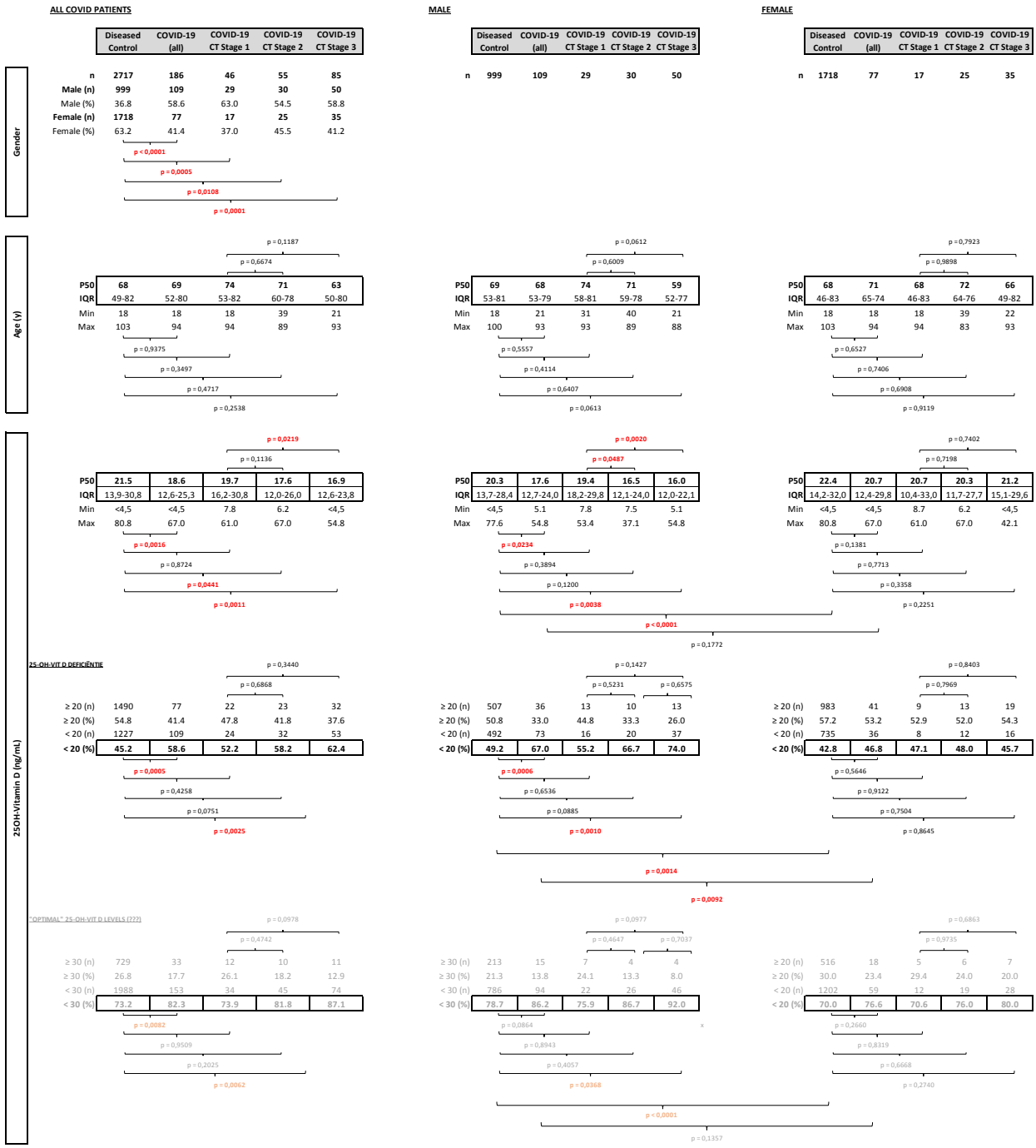
Supplementary Table S1: exact P values by Mann-Whitney test and Chi-squared test of 25(OH)D levels in COVID-19 patients (in support of Fig. 1 and Table 1)



statistical differences in median 25(0H)D levels accross groups calculated by Mann-Whitney test. Proportions for categorical variables were compared using the chi-squared test

Supplementary Table 2: Sex, age and seasonal variations in 25(OH) levels in 16,274 consecutive blood samples from in-and outpatients analyzed by the central laboratory of our tertiary hospital in 2019

Patient group	n (%)	Age, Median (IQR), y	25-OH-Vit D, Median (IQR), ng/mL	25-OH-Vit D < 20 ng/mL, n (%)
Gender distribution				
All	16274 (100)	64.2 (39.8-81.3)	23.3 (15.3-32.4)	6491 (39.9)
Female	10045 (61.7)	63.3 (37.4-82.0)	23.7 (15.6-33.1)	3875 (38.6)
Male	6229 (38.3)	65.2 (44.5-80.3)	22.3 (14.9-31.3) [a]	2616 (42.0) [b]
Age (year) distribution				
All				
≤ 1	113 (0.7)	0.7 (0.3-0.8)	44.4 (37.3-55.1)	6 (5.3)
1-10	761 (4.7)	5.0 (2.9-7.3)	32.7 (26.0-42.0)	83 (10.9)
10-18	399 (2.5)	13.1 (11.5-15.3)	23.9 (17.4-30.0)	130 (32.6)
18-30	1410 (8.7)	25.8 (22.6-27.9)	22.2 (15.5-30.0) [c, d]	600 (42.6) [e, f]
30-50	2842 (17.5)	40.1 (34.9-45.5)	22.5 (15.7-30.6) [c, d]	1171 (41.2) [e]
50-70	3727 (22.9)	60.1 (55.4-65.1)	23.4 (15.6-32.6) [c]	1467 (39.4) [e]
>70	7022 (43.1)	82.9 (77.5-87.7)	22.3 (13.9-31.9) [c, d]	3034 (43.2) [e, f]
Female				
≤ 1	49 (0.5)	0.7 (0.4-0.8)	44.8 (38.8-54.6)	4 (8.2)
1-10	360 (3.6)	5.5 (3.2-7.3)	32.9 (25.5-41.7)	33 (9.2)
10-18	240 (2.4)	13.6 (11.5-15.5)	23.3 (17.0-29.9) [g]	83 (34.6) [i]
18-30	1088 (10.8)	26.2 (23.1-28.0)	22.4 (15.6-30.1) [g, h]	455 (41.8) [i, j]
30-50	1862 (18.5)	39.1 (34.3-44.6)	22.9 (15.9-31.6) [g, h]	737 (39.6) [i]
50-70	2104 (20.9)	59.7 (55.2-64.8)	24.7 (16.5-34.2) [g]	766 (36.4) [i, j]
>70	4342 (43.2)	83.6 (78.2-88.1)	23.1 (14.0-32.9) [g, h]	1797 (41.4) [i]
Male				
≤ 1	64 (1.0)	0.6 (0.3-0.8)	44.3 (37.1-55.7)	2 (3.1)
1-10	401 (6.4)	4.7 (2.6-7.3)	32.1 (26.3-42.0)	50 (12.5)
10-18	159 (2.6)	12.8 (11.4-14.9)	24.5 (18.7-31.1)	47 (29.6)
18-30	322 (5.2)	24.4 (21.2-27.4)	21.6 (14.9-29.1) [k]	145 (45.0) [m]
30-50	980 (15.7)	41.7 (36.4-46.2)	21.8 (15.5-29.3) [k, l]	434 (44.3) [m, n]
50-70	1623 (26.1)	60.7 (55.6-65.5)	21.9 (14.4-30.7) [k, l]	701 (43.2) [m, n]
>70	2680 (43.0)	81.9 (76.5-86.7)	21.2 (13.8-30.1) [k, l]	1237 (46.2) [m, n]
Seasonal distribution				
Winter				
All	3889 (100)	62.5 (37.7-81.4)	21.8 (14.3-31.4) [o]	1740 (44.7) [q]
Female	2448 (62.9)	62.5 (36.1-81.3)	22.6 (14.5-32.4) [o]	1040 (42.5) [q]
Male	1441 (37.1)	62.8 (40.9-79.5)	20.4 (14.1-29.8) [o, p]	700 (48.6) [q, r]
Spring				
All	4277 (100)	65.8 (40.5-81.6)	22.2 (14.4-31.0) [o]	1832 (42.8) [q]
Female	2563 (59.9)	64.2 (37.3-82.0)	22.4 (14.8-31.6) [o]	1075 (41.9) [q]
Male	1714 (40.1)	67.5 (46.3-81.0)	21.8 (14.0-30.3) [o, p]	757 (44.2) [q]
Summer				
All	3619 (100)	63.3 (40.6-81.6)	25.7 (17.0-35.0)	1202 (33.2)
Female	2296 (63.4)	63.6 (38.8-82.5)	25.8 (17.2-35.4)	748 (32.6)
Male	1323 (36.6)	62.9 (43.3-80.1)	25.6 (16.7-34.2)	454 (34.3)
Fall				

All	4489 (100)	64.7 (40.1-80.9)	23.6 (15.9-32.6) [o]	1717 (38.3) [q]
Female	2738 (61.0)	63.1 (37.4-81.3)	24.2 (16.1-33.3) [o]	1012 (37.0) [q]
Male	1751 (39.0)	66.3 (45.7-80.3)	23.0 (15.6-31.3) [o, p]	705 (40.3) [q, r]

[a] 25-OH Vitamin D levels were significantly lower ($P < .0001$) in men than in women.
[b] Prevalence of 25-OH Vitamin D deficiency was significantly higher ($P < .0001$) in men than in women.
[c] 25-OH Vitamin D levels were significantly lower ($P < .05$) for all individual age groups > 18 years as compared with those aged ≤ 18 years.
[d] For all individuals aged > 18 years, subgroup 50-70 years showed significantly higher ($P < 0.05$) as compared with the other age groups.
[e] All age groups > 18 years showed significantly higher ($P < .05$) prevalence of 25-OH Vitamin D deficiency as compared with the individual age groups ≤ 18 years.
[f] For individuals aged > 18 years, subgroup 50-70 years showed significantly lower ($P < 0.05$) prevalence of 25-OH Vitamin D deficiency than the age groups 18-30 years and > 70 years.
[g] 25-OH Vitamin D levels were significantly lower ($P < .0001$) for female age groups > 10 years as compared with those aged ≤ 10 years.
[h] For women aged > 18 years, subgroup 50-70 years showed significantly higher ($P < 0.001$) 25-OH Vitamin D levels as compared with the other age groups.
[i] All female age groups > 10 years showed significantly higher ($P < .001$) prevalence of 25-OH Vitamin D deficiency as compared with the individual age groups ≤ 10 years.
[j] For women aged > 10 years, subgroups 10-18 years and 50-70 years showed significantly lower ($P < .05$) prevalence of 25-OH Vitamin D deficiency as compared with the other age groups.
[k] 25-OH Vitamin D levels were significantly lower ($P < .001$) for male age groups > 18 years as compared with those aged ≤ 18 years. Male age groups > 18 years did not show significant mutual differences.
[l] 25-OH Vitamin D levels were significantly lower ($P < .001$) for male age groups > 30 years as compared with female age groups > 30 years.
[m] All male age groups > 18 years showed significantly higher ($P < .001$) prevalence of 25-OH Vitamin D deficiency as compared with the individual age groups ≤ 18 years. Male age groups > 18 years did not show significant mutual differences.
[n] Male age groups 30-50 years, 50-70 years and > 70 years showed significantly higher prevalencesof 25-OH Vitamin D deficiency as compared with the female age groups (respectively $P < .05$, $P = .0001$ and $P < .0001$).
[o] For all patients and gender subgroups, 25-OH Vitamin D levels in winter and spring did not differ significantly. Winter-spring 25-OH Vitamin D levels were significantly lower as compared with summer ($P < .0001$) and fall ($P < .05$). 25-OH Vitamin D levels were significantly lower ($P < .0001$) in fall than those measured in summer.
[p] In all seasons, except for the summer, males have significantly lower 25-OH Vitamin D levels ($P < .05$) as compared with women.
[q] For all patients and female patients, prevalence of 25-OH Vitamin D deficiency in winter versus spring did not differ significantly. In contrast, male patients showed significantly higher ($P < .05$) prevalence of 25-OH Vitamin D deficiency in winter versus spring. For all patients and gender subgroups, winter-spring prevalence of 25-OH Vitamin D deficiency were significantly higher as compared with summer ($P < .001$) and fall ($P < .05$). 25-OH Vitamin D deficiency was significantly more prevalent ($P < .001$) in fall than in summer.
[r] In winter and fall, prevalence of 5-OH Vitamin D deficiency was significantly higher ($P < .05$) in men than in women.

Legend to Supplementary Table 2: Sex, age and seasonal variations in 25(OH) levels in 16,274 consecutive blood samples from in- and outpatients analyzed by the central laboratory of our tertiary hospital in 2019 We performed a retrospective analysis of serum 25(OH)D levels in N=16274 unselected and unique patients, composed from all consecutive blood samples analyzed from January 1; 2019 to December 31, 2019, in the central laboratory of our tertiary community hospital. Of note, this cohort cannot be considered representative for the general population, since all analyses were done for diagnostic purposes in subjects (60% outpatients, 40% inpatients) seeking medical care. A similar analysis on all consecutive 25(OH)D measurements in 2016, 2017 and 2018 give identical results, indicating that our sample of 16274 presents a reasonable proxy of vitamin D status in the population typically encountered in a mixed ambulatory and hospital group of patients. This analysis confirmed the known seasonal impact on 25(OH)D. In summary, this data shows that in 2019 samples from in- and outpatients ('diseased controls'): (i) All males showed lower median 25(OH)D levels and higher vitamin D deficiency (25(OH)D < 20 ng/mL) than females. A remarkably high fraction of patient samples (39.9%) showed vitamin D deficiency: 42% versus 38.6% in males versus females (P<0.05). (ii) Vitamin D deficiency rates were high in all age groups but clearly higher > 18 years versus 0-18 years, with the highest levels in patients > 70 years. (iii) We expectedly observed significantly lower 25(OH)D in winter and spring samples. This indeed shows that the first wave of SARS-CoV-2 infections hit our population in a timeframe with seasonally low 25(OH)D.

Supplementary Table 3. Demographic and comorbidity characteristics of diseased controls and COVID-19 patients and 25(OH) levels stratified by sex and radiological COVID-19 disease stage as compared to a season-matched cohort of pre-pandemic diseased controls sampled in March-April 2019

Patient group	Characteristic	Diseased Controls (March-April 2019)	All COVID-19 (March-April 2020)	COVID-19 (CT Stage 1)	COVID-19 (CT Stage 2)	COVID-19 (CT Stage 3)
All patients	n	**2717**	186	46	55	85
	Age, median (IQR), y	**68 (49-82)**	69 (52-80)	74 (53-82)	71 (60-78)	63 (50-80)
	Sex					
	Female, n (%)	**1718 (63.2)**	77 (41.4) †	17 (37.0) †	25 (45.5) †	35 (41.2) †
	Male, n (%)	**999 (36.8)**	109 (58.6) †	29 (63.0) †	30 (54.5) †	50 (58.8) †
	Comorbidity					
	Chronic lung disease, n (%)	**n.d.**	28 (15.1)	8 (17.4)	9 (16.4)	11 (12.9)
	Coronary artery disease, n (%)	**n.d.**	110 (59.1)	32 (69.6)	32 (58.2)	46 (54.1)
	Diabetes, n (%)	**n.d.**	26 (14.0)	9 (19.6)	7 (12.7)	10 (11.8)
	25-OH-Vitamin D					
	Median (IQR), ng/mL	**21.5 (13.9-20.8)**	18,6 (12.6-25.3) †	19.7 (16.2-30.8)	17.6 (12.0-26.0) †	16.9 (12.6-23.8) † ‡
	≥ 20 ng/mL, n (%)	**1490 (54.8)**	77 (41.4) †	22 (47.8)	23 (41.8)	32 (37.6) †
	< 20 ng/mL, n (%)	**1227 (45.2)**	109 (58.6) †	24 (52.2)	32 (58.2)	53 (62.4) †
Female patients	n	**1718**	77	17	25	35
	Age, median (IQR), y	**68 (46-83)**	71 (65-74)	68 (46-83)	72 (64-76)	66 (49-82)
	Comorbidity					
	Chronic lung disease, n (%)	**n.d.**	7 (9.1)	0 (0.0) §	3 (12.0)	4 (11.4)
	Coronary artery disease, n (%)	**n.d.**	43 (55.8)	11 (64.7)	13 (52.0)	19 (54.3)
	Diabetes, n (%)	**n.d.**	11 (14.3)	4 (23.5)	4 (16.0)	3 (8.6)
	25-OH-Vitamin D					
	Median (IQR), ng/mL	**22,4 (14.2-32.0)**	20.7 (12.4-29.8)	20.7 (10.4-33.0)	20.3 (11.7-27.7)	21.2 (15.1-29.6)
	≥ 20 ng/mL, n (%)	**983 (57.2)**	41 (53.2)	9 (52.9)	13 (52.0)	19 (54.3)
	< 20 ng/mL, n (%)	**735 (42.8)**	36 (46.8)	8 (47.1)	12 (48.0)	16 (45.7)
Male patients	n	**999**	109	29	30	50
	Age, median (IQR), y	**69 (53-81)**	68 (53-79)	74 (58-81)	71 (59-78)	59 (52-77)
	Comorbidity					
	Chronic lung disease, n (%)	**n.d.**	21 (19.3)	8 (27.6) §	6 (20.0)	7 (14.0)
	Coronary artery disease, n (%)	**n.d.**	67 (61.5)	21 (72.4)	19 (63.3)	27 (54.0)
	Diabetes, n (%)	**n.d.**	5 (13.8)	5 (17.2)	3 (10.0)	7 (14.0)
	25-OH-Vitamin D					
	Median (IQR), ng/mL	**20.3 (13.7-28.4)**	17.6 (12.7-24.0) †	19.4 (18.2-29.8)	16.5 (12.1-24.0) ‡	16.0 (12.0-22.1) † ‡
	≥ 20 ng/mL, n (%)	**507 (50.8)**	36 (33.0) †	13 (44.8)	10 (33.3)	13 (26.0) †
	< 20 ng/mL, n (%)	**492 (49.2)**	73 (67.0) †	16 (55.2)	20 (66.7)	37 (74.0) †

† Indicates differences with diseased controls for which P values less than .05 were considered statistically significant.
‡ Indicates differences with CT Stage 1 COVID-19 patients for which P values less than .05 were considered statistically significant.
§ Indicates differences of male vs female comorbidity prevalence for which P values less than .05 were considered statistically significant.

Legend to Supplementary Table 3: We additionally compared the 25(OH)D levels in 186 COVID-19 patients (sampled from March 1, 2020 to April 7,2020) to a seasonally-matched historical cohort, subsampled from the 16274 samples: we selected consecutive 25(OH)D measurements in patient

samples, measured between March 1, 2019 to April 30, 2019: this gave 2717 data points (indicated in bold font as 'Diseased controls'). We stratified those data for sex to account for the over-representation of males in our COVID-19 cohort. No clinical meta-data and registration of comorbidities was available for this cohort. This retrospective analysis indicated that (i) Median 25(OH)D at intake in COVID-19 patients were lower than in season-matched diseased controls: 18,6 (12.6-25.3) versus 21.5 (13.9-20.8) ($P<0.05$). COVID-19 patients showed higher rates of vitamin D deficiency on admission than season-matched diseased controls (59% versus 45%) ($P<0.05$). (ii) Stratification for sex indicated that the male COVID-19 patients were most affected: male COVID-19 patients showed lower median 25(OH)D (17.6 versus 20.3 ng/mL) levels and higher rates of vitamin D deficiency (67% versus 49%) than season-matched male diseased controls (both $P<0.05$).

Supplementary methods: detailed CT scanning protocol

All patients were imaged by MDCT using either of the following CT scanners: the GE LightSpeed VCT scanner (1-mm slice thickness), Siemens Somatom AS (1-mm slice thickness) or the GE Optmima 660 scanner (1.25-mm slice thickness). All scans were performed without intravenous contrast with the patient in the supine position during end-inspiration. Only the initial CTs were included; follow-up CTs during the study time window were not analyzed.

Image Viewing and Evaluation Two cardiothoracic radiologists with 24 and 9 years of experience retrospectively reviewed the CT exams on a PACS workstation (IDS7, Sectra) with multiplanar reconstruction tools. Decision was reached by consensus.

For each patient, the chest CT scan was evaluated for the following characteristics:

(1) presence of ground-glass opacities (early stage, "**stage 1**")

(2) presence of crazy paving pattern (progressive stage, "**stage 2**")

(3) presence of consolidation (peak stage, "**stage 3**")

(4) number of lobes affected where either ground-glass / consolidative opacities were present,

(5) degree of involvement of each lung lobe in addition to overall extent of lung involvement measured by means of a "CT-severity score" as detailed below

(6) presence of a pleural effusion

(7) presence of pericardial effusion

(8) presence of thoracic lymphadenopathy (defined as lymph node size of ≥10 mm in short-axis dimension)

(10) airways abnormalities (including bronchiectasis, bronchial wall thickening and endoluminal secretions)

(11) craniocaudal and anteroposterior distribution of disease

(12) **presence of underlying chronic lung disease** such as emphysema or fibrosis

(13) presence of **coronary artery disease** as measured by coronary artery calcium scoring, a marker of atherosclerotic plaque burden and independent predictor of myocardial infarction and mortality.

Each of the five lung lobes was assessed for degree of involvement and classified as none (0%), discrete (<5%), minimal (5 - 25%), mild (26 - 50%), moderate (51 - 75%), or severe (> 75%). No involvement corresponded to a lobe score of 0, discrete to a lobe score of 1, minimal to a lobe score of 2, mild to a lobe score of 3, moderate to a lobe score of 4, and severe to a lobe score of 5. An overall lung "CT-severity score" was reached by summing the five lobe scores (range of possible scores, 0 - 25). CT-severity score was not used in the current study.

The stage was estimated by consensus evaluation of the predominant radiological presentation: ground-glass opacities (early stage, 0-4 days, "stage 1"), (2) presence of crazy paving pattern (progressive stage, 5-8 days, "stage 2"), (3) presence of consolidation (peak stage, 10-13 days, "stage 3") [1, 2]

References

1. Bernheim A, Mei X, Huang M, et al. Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to Duration of Infection. Radiology. 2020:200463.
2. De Smet K, De Smet D, Ryckaert T, et al. Diagnostic Performance of Chest CT for SARS-CoV-2 Infection in Individuals with or without COVID-19 Symptoms. Radiology. 2020:202708.